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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,670	03/19/2001	Akiko Itai	P20797	9032

7055 7590 06/16/2005

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EXAMINER
MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,670	ITAI ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5-0-0

Information Disclosure Statement

The information disclosure statement filed 5/23/05 has been considered. WO 96/13785 was considered as part of the IDS filed 11/14/01 and has been crossed out to avoid duplication upon printing. It is noted that the reference by TOMIOKA is in Japanese and is not accompanied by a translation, and thus has been considered only to the extent of the relevance indicated in the response filed 3/23/05; i.e. that it was listed in a search report for a corresponding International application. Applicant is thanked for providing copies of the missing references and the search report.

Claim Objections

The objection to claims 1-3 are hereby withdrawn in view of the claim amendments filed 3/23/05.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-10 are directed to methods for selecting lead-candidate compounds capable of binding to a biopolymer. Claims 1 and 10 recite steps of obtaining data and selecting a trial compound. Claims 2-7 recite further in silico steps. These steps are ones of mathematical manipulation, equivalent to mental processes. Where a claim

recites mental processes in the absence of a concrete, tangible and useful result, the claim is not directed to statutory subject matter. See MPEP 2106, as previously indicated in the office action of 9/23/04.

None of the claims recites any physical method step (i.e. a "safe harbor") nor any step of transforming data which would render the claims statutory. It is unclear what the actual result of the claimed methods is intended to be (see below), therefore the claims do not recite a concrete, tangible and useful result. Claim 1 now recites steps of "selecting" a compound or molecule. However, as the result of the method is not output or otherwise communicated to a user, the method does not produce a result in a form which is concrete, tangible and useful. For these reasons, the claimed methods are not statutory.

Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The claims are directed to methods for selecting lead-candidate compounds capable of binding to a biopolymer "for use as a physiologically active compound", but claims 1-10 fail to actually recite any step of selecting a lead compound nor a compound which is "physiologically active." Claims 1 and 10 recite steps of selecting a query molecule and at least one trial molecule, but fail to recite any actual step of selecting a "lead compound" which would be "useful" as a "physiologically active compound", as claimed. As no "lead compound" with any sort of activity is actually selected, the claims do not produce an "immediately useful" result. In addition, in the

absence of any knowledge with regard to the "physiological" activity desired, selection of a compound with such activity does not provide utility to the method.. What is the "immediate benefit" to one of skill in the art of determining that a compound MAY have an unidentified activity? Applicant is reminded that a "use" to do further research is not a utility under 35 USC 101. For the reasons set forth above, the claims lack utility.

Applicant's arguments filed 3/23/05 have been fully considered but they are not persuasive. In response to the argument that selecting a lead compound is a concrete, tangible and useful result, it is noted, as set forth above, that the claims do not recite a step of actually selecting a lead compound. In response to the argument that the claims recite "on active transforming process", it is noted that steps of obtaining a database and selecting compounds are neither physical steps nor steps of transforming data. Applicant does not specifically point to a step which is the 'active transforming process" in the response. For these reasons, the arguments are not persuasive, and the claims are rejected.

Claim Rejections - 35 USC § 112, 1st para.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following includes both a lack of enablement and a lack of scope of enablement rejection.

The claims are not enabled for SELECTION of a lead-candidate compound which binds to any type of biopolymer because neither the specification nor the prior art teach specific parameters for selection of a compound or compounds which bind to any (generic) biopolymer.

Claims 1-10 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying compounds which may bind to proteins such as dihydrofolate reductase, does not reasonably provide enablement for identifying compounds which bind to any other type of biopolymer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Where the claims read on merely identifying compounds capable of binding to a biopolymer, the claims are enabled for identifying compounds which may bind to proteins such as dihydrofolate reductase because the specification teaches how to perform docking assays with proteins found in structural databases such as the Cambridge Crystallographic Database (CCD) or the Brookhaven Protein Data Bank (PDB), but are not enabled for identifying compounds which bind to any other type of biopolymer because neither the specification nor the prior art teach how to do so.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC

1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

The claims are quite broad as they are directed to selection of a lead-candidate compound capable of "interacting" with any type of biopolymer. The claims may also be interpreted broadly as merely identifying compounds which bind to, participate in ionic interactions with, participate in hydrophobic interactions with, etc. a biopolymer. The specification teaches, in examples, how to determine/identify compounds likely to bind to a protein, specifically dihydrofolate reductase. The specification does not teach particular conditions which must be met to select a compound as a "lead-candidate"; i.e. to single out any particular compound as being a "better" ligand than the others, or which binds more tightly than another, etc. The state of the prior art is such that docking programs for "fitting" a ligand into a binding site of a protein are known. See e.g. DESJARLAIS et al. (IDS ref: J. Med. Chem. (1988) vol. 31, pp. 722-729). DESJARLAIS teaches specific steps for "scoring" the fit between a receptor and candidate compounds and teaches on page 724 that a user may "select the number of top scoring candidates" to be saved for further energy minimization steps. It is noted that the claimed methods do not recite any particular steps of scoring or ranking candidate compounds similar to those of DESJARLAIS, such that a selection may be made of the "top" candidates. It is further noted that DESJARLAIS teaches fitting only to proteins wherein the crystallographic structure is known (pp. 726-727). The prior art of NISHIBATA (IDS ref: Tetrahedron (1991) vol. 47, no. 43, pp. 8985-8990) teaches

design of drug candidates based on the KNOWN structure of protein receptors using the LORE program. Again, NISHIBATA teaches use of a protein with known crystallographic coordinates (p. 8987) and does not teach design of candidate compounds which bind to any other type of biopolymer. In addition, NISHIBATA teaches specific parameters for selection of nine "lead-candidate" structures from among the 300 possible structures generated (pp. 8987-8989). The instant specification teaches "use" of similar parameters (e.g. information about atomic types and mode of covalent bonding), but fails to disclose any specific parameters which would allow on of skill in the art to know WHAT to select. For example, what kind of "atomic types" are to be excluded or included in the selection step? Which covalent bonds are to be considered? Are certain types of bonds excluded, included, or perhaps weighted? Claim 1 recites "matching" information on atomic types and covalent interactions from a database of query molecules to trial compounds to select a trial compound, but fails to recite what degree, if any, of similarity is required for a "match" . Neither the instant claims nor the specification disclose which parameters are to be used to determine "matching".

The level of skill in the art of docking/fitting is acknowledged to be high. Despite this, it would require undue experimentation for one of skill in the art to identify any compound capable of binding to a biopolymer other than a protein because such a method is not taught by the instant specification of the prior art, as set forth above. Further, it would require guesswork by a skilled practitioner to determine how to *select* a "lead-candidate" capable of binding to a protein or any other type of biopolymer

because neither the specification nor the prior art teach conditions or parameters for selection which are universal to all biopolymers. Conditions for determining the "best" or "lead" compounds depend on which algorithm is used, what type of protein is chosen, and what type of activity one is looking for in a "lead" compound (i.e. binding alone? tightness of fit? lowest energy? similarity to other (known) drugs? etc.). As one of skill in the art would have to guess at the parameters involved in selection and/or "matching" to a query molecule, this would require undue experimentation.

For the reasons set forth above, the claims are not enabled for selection of lead-candidate compounds of any type, and are enabled only for identification of compounds capable of binding to proteins, but not to any other type of biopolymer.

Applicant's arguments filed 3/23/05 have been fully considered but they are not persuasive. Applicant argues on pages 13-14 of the response that one skilled in the art would know how to select a lead compound based atomic types and covalent bonds of compounds. In response, it is noted that the claims fail to recite any step of actually selecting a lead compound, and that parameters for selecting a compound as a LEAD (i.e. one which is "better" or has more "desirable" properties than others) are not disclosed anywhere. Applicant further argues that one skilled in the art would know how to select a lead compound by matching a query molecule with compounds stored in a database, wherein the database contains information on atomic types and covalent bonds. It is admitted that one skilled in the art would know how to obtain or calculate atomic and binding information, and would know how to COMPARE information for a specific molecule to information from a database. However, the examiner maintains

that as the specification fails to teach one skilled in the art what parameters are required to determine how to "match" a query molecule to information in the database, one skilled in the art must guess at such parameters; e.g. does a "match" require 100% congruence between molecules for atomic types and covalent bonds, less than 100% (if so, what percentage of congruence is required?), 100% over a portion of a molecule, are some covalent bonds weighted more than others in determining a match, etc? This constitutes undue experimentation, therefore the examiner maintains that the claims lack enablement.

With regard to the lack of scope of enablement, applicant argues that the claimed method is enabled for identifying compounds which may bind to biopolymers other than proteins such as dihydrofolate reductase because the specification defines biopolymers and the claims are now limited to selecting lead compounds from a database comprising information on atomic types and covalent bonds. In response, applicant is reminded that the claims are rejected for lack of enablement, not for lack of written description or lack of clarity. The fact that the term "biopolymer" is defined broadly does not enable the full scope of the claims. It is noted that the term "biopolymer", as defined by the specification , encompasses polysaccharides, lipid chains, and oligonucleotides. Neither the prior art nor the instant specification teaches how to select a lead compound, for example, from a database comprising bond and atomic information for polysaccharides or lipid chains. For these reasons, the examiner maintains that the claims are not enabled for their full scope.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

A step of "modifying" a structure, as recited in amended claim 2, is new matter. Original claim 2 limited compounds to be "modified" such that their binding to a biopolymer "should not be retarded", thus limiting the modification to result in a compound which has binding equal to or "better" than a template compound. Amended claim 2 does not so limit the modification step. The original specification, on page 5, replicates the terminology of original claim 2, but does not disclose general "modification" of a structure anywhere. Applicant does not point to support for the new limitation in the response filed 3/23/05. As the limitation of amended claim 2 is broader than that originally recited, and support for the broader limitation is not found in the originally field disclosure, as et forth above, claim 2 is rejected.

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This a LACK OF WRITTEN DESCRIPTION rejection.

Claim 4 recites "the algorithm of Ullman" in line 3. The original claims did not recite this limitation. The originally filed specification refers to an algorithm by "Ullman" on page 11, thus this limitation is not new matter. However, the specification does not set forth the actual algorithm anywhere. The reference cited on page 11 is not incorporated by reference, thus the reference is not part of the disclosure. As the instant specification fails to disclose the actual algorithm of Ullman, claim 4 is rejected for lack of written description. Applicant is advised that as the reference was not incorporated by reference at the time of filing of the instant specification, it is not considered part of the originally filed disclosure.

Claim Rejections - 35 USC § 112, 2nd para.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 10 recite methods for selecting a lead candidate compound, and recite functional limitations of the compound, in the preamble. However, the claim steps do not recite selection of a lead candidate compound, nor of any compound with the function recited in the preamble. The claims appear to be missing an element or nexus between the preamble and actual steps, thus the claims are indefinite.

Claim 2 recites a step of "modifying" the structure of a query molecule. It is unclear what type or level of modification is intended; i.e. modification of glycosylation sites/levels, deletions, insertions, substitutions, some combination of the preceding, etc. As the metes and bounds intended by applicant for "modifying" the structure of a query molecule are unclear, the claims are indefinite.

Claim 4 recites "the algorithm of Ullman" in line 3. There is no antecedent basis for this term in the claims, therefore use of the term renders the claims indefinite. Further, while the specification refers to an algorithm by "Ullman" on page 11.

Claim 6 limits a step (a) to comprise steps (c) and (d); however, no step (b) is recited. It is unclear if the claims are missing an intermediate step (b), therefore claim 6 is indefinite. It is noted that claim 5 recites a step (b); however, claim 6 does not depend from claim 5. In addition, the step (b) of claim 5 presumable follows step (a) whereas steps (c) and (d) are clearly limited to be part of step (a).

Claim 8 limits the method of claim 3 to further comprise a "third screening" comprising a step (f) and/or a step (g). As claim 3 recites only a step of selecting and does not recite any step of screening, it is unclear what is meant by the "third screening" limitation of claim 8, therefore claim 8 is indefinite. Further, claim 3 recites only a step (a). Recitation of steps (f) and (g), with no other intervening steps, in claim 8 renders it unclear whether other steps are intended, or are missing, from the claims, therefore claim 8 is further indefinite.

Claim Rejections - 35 USC § 102

The rejections made under 35 USC 102 are hereby withdrawn in view of the amendment filed 3/23/05.

Conclusion

Claims 1-10 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
6/10/05